

## Special Article

### CONCERNING THE ETIOLOGY AND TREATMENT OF MEASLES

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*THE EDITOR: Reports of the California State Board of Health which show that we are in the midst of an epidemic of measles that is widely distributed over the state makes it fitting to publish a brief review of recent investigations concerning the etiology and specific treatment of this disease. Such a review, prepared at our request by Ernest C. Dickson, Professor of Public Health, Stanford University Medical School, is submitted.*

**SEARCH** for the infectious agent in measles has been going on for many years. In 1758 Home<sup>1</sup> in Edinburgh and Herne<sup>2</sup> in France believed that they had demonstrated that measles could be transferred from a patient to susceptible children by means of cotton which was soaked with the blood of the patient and applied to incisions in the arm of the susceptibles. There is some doubt as to whether they really produced measles, although several investigators have reported that they confirmed their observations. However, in 1905, Hektoen<sup>3</sup> proved that measles can be transferred from patients to susceptibles by injecting blood of the patients into the veins of the susceptibles, and showed that the virus is present in the blood at least twenty-four hours before and thirty hours after the appearance of the rash.

In 1917 Tunncliff<sup>4</sup> reported the isolation from the blood of measles patients of a minute, filter passing, diplococcus which produces a green pigment, and she later showed that the same organism can be cultivated from the secretions of the respiratory tract at the same time as it is present in the blood. Specific antibodies for this organism can be demonstrated in the serum of patients who are convalescent from measles, and skin tests, analogous to the Schick test and the Dick test, can be demonstrated in susceptible individuals. Moreover, Tunncliff and her associates<sup>4</sup> showed that a disease which closely resembles measles can be produced in monkeys, rabbits, and guinea-pigs, by injecting them with this diplococcus.

Several investigators, notably Thomson,<sup>5</sup> Caronia,<sup>6</sup> and Ferry and Fisher,<sup>7</sup> have also isolated diplococci which appear to differ somewhat from those described by Tunncliff, but still others<sup>8</sup> have confirmed Tunncliff's observations, and Hoyne and Gasul<sup>9</sup> believe that the apparent differences are due to differences in cultural methods, and that all are really dealing with the same organisms.

Be that as it may, the evidence is strongly indicative that Tunncliff, and probably the other investigators have established the bacterial cause of measles.

#### PROPHYLAXIS

Of more immediate interest to medical practitioners, however, is the work which is being done along the lines of prophylaxis and specific therapy of measles. This is being followed along two lines: (1) to induce the formation of antibodies by the individual himself; active immunization, and (2)

to develop means by which antibodies can be supplied to him when he needs them: passive immunization.

#### ACTIVE IMMUNIZATION

Attempts to induce active immunization of children who are susceptible to measles have not progressed beyond the realm of experiment, and this method cannot as yet be recommended for general application.

Investigators have approached the problem mainly along three lines:

1. It is well known that infants born of mothers who are immune to certain of the communicable diseases passively acquire antibodies from their mother's blood through the placenta, and that for four to six months after birth they are relatively resistant to these diseases.

Herrman<sup>10</sup> sought to take advantage of this temporary passive immunity to measles and recommended that infants should be inoculated with measles by the transfer of measles virus from the nasopharynx of a patient to the nasopharynx of the infant. His object was to stimulate active immunization of the infant by injection which would be very mild because of the presence of the mother's antibodies. The method is obviously impractical, and in many ways objectionable, particularly in family practice.

2. Hiraishi and Okamoto<sup>11</sup> and Debré and his associates<sup>12</sup> recommended repeated injections of minute quantities of blood from measles patients, taken during the early stages of the disease when the blood contains living virus. Their results have not been uniform.

3. Sindoni,<sup>13</sup> an associate of Caronia, prepared bacterial vaccines from the diplococcus which Caronia<sup>6</sup> isolated from measles patients and gave repeated injections of the vaccine to susceptible children. He concluded that the results were of sufficient promise to justify further investigation.

#### PASSIVE IMMUNIZATION

##### (a) Use of convalescent serum.

In 1916 Nicolle and Conseil<sup>14</sup> succeeded in protecting susceptible children from measles by injecting small quantities of blood serum or whole blood from patients who were convalescent from measles. Their report was published in 1918, and in that year Richardson and Connor<sup>15</sup> reported similar satisfactory results from a group of tests in Boston. Park and Zingher, in New York, commenced their observations in 1916 and have done much to develop this method of prophylaxis.

Zingher in 1924<sup>16</sup> reviewed the work which had been done and reported a series of cases, and in 1926 Park and Freeman<sup>17</sup> brought the report from New York to date. These investigators found that among 753 cases treated in institutions, 84 per cent showed completely successful results; that is, the children did not develop measles after contact, whereas 95 per cent showed some degree of benefit, either complete protection from the disease, or marked attenuation of the severity of illness. In family practice, among 226 cases, the results were less satisfactory, only 52 per cent of children re-

maintaining free from measles although 95 per cent were more or less benefited.

Many other investigators have reported similar results, and there are no records of ill effects when care is taken to ascertain that the donors are free from syphilis, tuberculosis, and other communicable diseases.

The dose of immune serum as recommended by Park and Freeman<sup>17</sup> is 6 cc. of serum or plasma for children under 3 years of age and 6-10 cc. for children over three. The antibody content of the serum is greatest within a few days after convalescence, but is still relatively high for at least a month. Rietschl<sup>18</sup> recommended that serum from adults who have had measles may be used, but the dose required is much larger than when convalescent serum is used and the results are much less uniform. When whole blood is used instead of serum, double the stated dose for serum should be administered and Zingher<sup>16</sup> states that this is not damaged by the addition of citrate and may be given intramuscularly.

Park and Freeman<sup>17</sup> report that if the serum is given within three days after exposure to infection the onset of the disease is prevented in the great majority of cases, and if on the fourth or fifth day, the course of the disease is mild and complications are unusual. Zingher<sup>16</sup> recommended larger doses for late administration, 7.5 cc. for children 3 years old on the seventh or eighth day being sufficient to ameliorate the course of the disease.

The duration of immunity from convalescent serum is from two to four weeks, after which the child is again susceptible to measles. It follows that its use is of greatest value in children under 3 years of age in whom the mortality from measles is very high, and in debilitated children or those suffering from other types of disease which might endanger their recovery. In older children it is recommended by some that only sufficient serum be administered to insure a mild attack of the disease as it is by actual infection that active immunization and subsequent resistance to infection can be obtained.

#### ANTITOXIC SERUM

Various investigators have attempted to produce an antitoxin which can be produced commercially since, at best, the available supply of immune serum must be limited. Tunncliffe and Hoyne<sup>19</sup> have recently reported successful immunization of goats with the production of a serum which has proved to be highly potent. They found that 97 per cent of individuals over 1 year of age and 98 per cent of infants less than 1 year of age were protected from measles if the goat serum was given within three days of exposure to infection, and that 45 per cent of cases over 1 year old were protected if they received the serum on the fourth day. They employed goat serum in order that there might not be sensitization to horse serum, which is the vehicle of diphtheria and scarlet fever antitoxin, and reported only 12 per cent of cases of serum disease.

These observations are of utmost importance because they indicate that in the near future we may have specific antitoxin for the treatment of measles. It should be remembered, however, that the work

is still in the experimental stage and that it may be some time before commercial serum is on a par with that for the treatment of diphtheria.

#### REFERENCES

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**Cass Treatment for Rheumatism (Propaganda for Reform)**—One hundred and thirty-seven West Sixty-second Street, Chicago, houses a choice line of quackery. Under the names "Western Medical Association" and "Vernon Laboratories" a fake "epilepsy cure" is exploited on the mail-order plan. Under the name "Cass Laboratories," nostrums for rheumatism, sciatica, neuralgia, lumbago, and gout are sold—also through the United States mails. The A. M. A. Chemical Laboratory reports that the "Cass treatment" consists of pink tablets, "Special Saline Compound" and gray tablets. The laboratory found the pink tablets to contain 0.6 Gm. of sodium bicarbonate per tablet. The "Special Saline Compound" was found to be essentially flavored magnesium sulphate. The gray tablets were found to contain essentially 0.16 Gm. acetylsalicylic acid, 0.13 Gm. cinchophen and 0.3 Gm. charcoal per tablet. From the laboratory's report it is seen that this wonderful discovery "developed under the direction of the head professor of chemistry at one of the nation's largest universities," and declared by "two of the foremost medical scientists in this country" to be superior to anything else in its line, is merely a combination of acetylsalicylic acid and cinchophen with sodium bicarbonate and magnesium sulphate.—*Journal A. M. A.*, January 15, 1927.

**Physical Therapy and Pseudophysics (Propaganda for Reform)**—Much of the literature on physical therapy has apparently been written with an eye to the royalty statement or the publicity returns rather than to the possibility of scientific criticism. These treatises become impressive, in size at least, by the inclusion of statements on the physics of the apparatus culled almost in toto from the advertising and descriptive matter published by a manufacturer. This practice might be commendable if the physical concepts were not often wholly at variance with the concepts generally accepted by physicists. The physician who desires a substantial knowledge of physical therapy must choose his sources of information carefully.—*Journal A. M. A.*, January 15, 1927.